The pediatric Rome IV criteria: what’s new?

Ilan J.N. Koppen, Samuel Nurko, Miguel Saps, Carlo Di Lorenzo & Marc A. Benninga


To link to this article: http://dx.doi.org/10.1080/17474124.2017.1282820

© 2017 The Author(s). Published by Informa UK Limited, trading as Taylor & Francis Group

Accepted author version posted online: 16 Jan 2017.
Published online: 24 Jan 2017.

Submit your article to this journal

Article views: 2703

View related articles

View Crossmark data

Citing articles: 1 View citing articles
The pediatric Rome IV criteria: what's new?

Ilan J.N. Koppen\textsuperscript{a}, Samuel Nurko\textsuperscript{b}, Miguel Saps\textsuperscript{c}, Carlo Di Lorenzo\textsuperscript{c} and Marc A. Benninga\textsuperscript{a}

\textsuperscript{a}Department of Pediatric Gastroenterology and Nutrition, Emma Children’s Hospital / Academic Medical Center, Amsterdam, the Netherlands; \textsuperscript{b}Center for Motility and Functional Gastrointestinal Disorders, Boston Children’s Hospital, Boston, MA, United States of America; \textsuperscript{c}Division of Pediatric Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, Nationwide Children’s Hospital, Columbus, OH, United States of America

\textbf{ABSTRACT}

\textbf{Introduction}: Functional gastrointestinal disorders (FGIDs) are common in children of all ages and comprise a wide range of conditions related to the gastrointestinal tract that cannot be attributed to structural or biochemical abnormalities. FGIDs are diagnosed according to the symptom-based Rome criteria. These are revised in Rome IV, which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited, and is not altered, transformed, or built upon in any way.

\textbf{Areas covered}: In 2016, the revised pediatric Rome IV criteria were published, these revised criteria are discussed in this review article. For the youngest age group (neonates/toddlers), the criteria for infant colic have undergone the most notable revisions. The most prominent changes in Rome IV were made in the criteria for children/adolescents, with the definition of two new FGIDs (functional nausea and vomiting) and the restructuring of the criteria for functional abdominal pain disorders, including the definition of FGID subtypes for functional dyspepsia and irritable bowel syndrome.

\textbf{Expert commentary}: Overall, the Rome IV have been refined and are expected to improve the process of diagnosing FGIDs in the pediatric population and to better facilitate the healthcare professional in distinguishing different clinical entities. These changes will likely benefit future research and clinical care.

1. Introduction

1.1. The road that led to Rome

Functional gastrointestinal disorders (FGIDs) are common in children of all ages and comprise a range of disorders that are considered to be related to the gastrointestinal tract, but cannot be explained by structural or biochemical abnormalities [1,2]. Symptoms related to these FGIDs have a significant impact on families, the patient’s quality of life and health care utilization and related costs [3–6].

In children, FGIDs are diagnosed according to the symptom-based Rome criteria, which have been developed by working committees of the Rome Foundation through literature review and a consensus process. The Rome criteria for FGIDs were first established in 1990, and these were only applicable in adults. In 1999, with the launch of the Rome II criteria, criteria were established for FGIDs in children. At that time there was a paucity of literature regarding FGIDs in children and for some diagnoses, the criteria mimicked the standards assembled by the adult gastroenterologists. These were revised in 2006, with the launch of the Rome III criteria and recently, in 2016, the revised Rome IV criteria were published. Since the Rome III publication, a distinction has been made between FGIDs in younger (neonate/toddler) and older children (child/adolescent). Tables 1 and 2 list the Rome IV diagnoses for children in both of these age groups and Figure 1 shows a timeline depicting the age at which FGIDs occur.

1.2. Why do we need the Rome criteria?

One of the difficulties in dealing with FGIDs is that there are no biochemical markers or structural abnormalities that can be used to objectively diagnose or monitor progression of these disorders. Diagnoses are based on medical history and physical examination. It is essential that these symptom-based diagnostic criteria are accurate, clear, and unambiguous. For clinicians, it is important that these criteria are easy to use and enable them to adequately evaluate and diagnose children so that testing is minimized and appropriate treatment is implemented. For patients and caregivers, clear and predefined diagnoses may help to better understand and accept the diagnosis of an FGID despite the absence of demonstrable underlying organic pathology. Uniform diagnostic criteria are also necessary to conduct reliable, reproducible research on the epidemiology, pathophysiology and management of FGIDs in children.

2. What is new in Rome IV?

Recent insights into the epidemiology, pathophysiology, diagnostic workup, and treatment of FGIDs have resulted in several changes in the Rome IV criteria, compared to the Rome III...
In this review, we will discuss the most significant changes in Rome IV, their clinical implications, and future perspectives. The Rome IV criteria for neonates/toddlers and children/adolescents are provided in Appendices 1 & 2.

2.1. Neonates/toddlers

Diagnosing FGIDs in young children, who cannot report symptoms accurately, is mainly based on parental report and their interpretations of the child’s symptoms. This makes it challenging to define criteria for FGIDs in this age group. For the diagnoses infant regurgitation, infant rumination syndrome, and cyclic vomiting syndrome, the wording of the criteria has been changed to address the difficulty in assessing complex symptoms in young children, e.g. the inability to adequately report nausea or pain. Aside from textual alterations and minor modifications concerning time criteria, the aforementioned diagnoses were not changed significantly. For infant colic, however, the criteria have undergone major revisions. The working committee has abandoned Wessel et al.’s ‘rule of threes’ (crying more than 3 h a day, for more than 3 days a week, for more than 3 weeks in a row) as a requirement for the diagnosis. Instead of using these arbitrary limits for the amount of crying, the criteria are now focused on factors that have been shown to cause distress in parents, i.e. the prolonged, hard-to-soothe, and unexplained nature of the crying behavior. Furthermore, more specific diagnostic criteria have been added for clinical research purposes.

New insights into the defecation pattern of young children have led to changes in Rome IV. Based on a survey study among parents of young children in the USA [7], the defecation frequency required for the diagnosis of functional diarrhea has changed from 3 to 4 stools per day. Moreover, the passing of stools during sleep has been removed from these criteria because of its low specificity. Another diagnosis that has undergone changes is infant dyschezia. Based on a recent prospective study showing that this disorder can be present up to the age of 9 months, the age limit has been modified [8]. Moreover, the straining and crying that are characteristic for

| Table 1. Functional gastrointestinal disorders in neonates and toddlers. |
|-----------------------------|-----------------------------|
| G1  | Infant regurgitation        |
| G2  | Infant rumination syndrome  |
| G3  | Cyclic vomiting syndrome    |
| G4  | Infant colic                |
| G5  | Functional diarrhea         |
| G6  | Infant dyschezia            |
| G7  | Functional constipation      |

Reprinted from Gastroenterology, 150(6), Benninga, M. A., et al., Childhood Functional Gastrointestinal Disorders: Neonate/Toddler, pp. 1443–1453, copyright (2016), with permission from Elsevier [1].

| Table 2. Functional gastrointestinal disorders: children and adolescents. |
|-----------------------------|-----------------------------|
| H1. Functional nausea and vomiting disorders                      |
| H1a. Cyclic vomiting syndrome                                      |
| H1b. Functional nausea and functional vomiting                     |
| H1c. Rumination syndrome                                            |
| H1d. Aerophagia                                                     |
| H2. Functional abdominal pain disorders                             |
| H2a. Functional dyspepsia                                           |
| H2b. Irritable bowel syndrome                                       |
| H2c. Abdominal migraine                                            |
| H2d. Functional abdominal pain – not otherwise specified           |
| H3. Functional defecation disorders                                 |
| H3a. Functional constipation                                        |
| H3b. Nonretentive fecal incontinence                                |

Reprinted from Gastroenterology, 150(6), Jeffrey, S., et al., Childhood Functional Gastrointestinal Disorders: Child/Adolescent, pp. 1456–1468, copyright (2016), with permission from Elsevier [2].

criteria. In this review, we will discuss the most significant changes in Rome IV, their clinical implications, and future perspectives. The Rome IV criteria for neonates/toddlers and children/adolescents are provided in Appendices 1 & 2.
this disorder are no longer required to precede a successful passage of stools, but may also be associated with an unsuccessful passage of stools.

For functional constipation, a differentiation has now been made between children who are toilet trained and children who are not. This was done for practical purposes, e.g. the unreliable assessment of the presence of fecal incontinence in children wearing diapers.

Furthermore, Rome IV addresses the neurobiology of pain, assessing the neurodevelopment of nociception and discussing an array of factors that impact the pain experience.

2.2. Children/adolescents

For children and adolescents, FGIDs are divided into three main groups: functional nausea and vomiting disorders, functional abdominal pain disorders and functional defecation disorders. For these disorders, it is now specified that the diagnosis can only be made if ‘after appropriate medical evaluation, the symptoms cannot be attributed to another medical condition.’ This wording substitutes the previous statement that there had to be ‘absence of inflammatory, anatomic, metabolic, or neoplastic process that explains the subject’s symptoms.’ This change allows a patient with another organic disease, such as celiac disease or inflammatory bowel disease for example, to have a functional disorder as well (a common event) and should also reduce the amount of testing needed to make the diagnosis of a FGID.

2.2.1. Functional nausea and vomiting disorders

The paramount change in this group of FGIDs is the establishment of the clinical entities of functional nausea and functional vomiting. These are new diagnoses that were not described in the Rome III criteria. For the diagnosis of functional nausea, children must suffer from bothersome nausea as the predominant symptom at least twice a week for at least 2 months, and this symptom is generally not related to meals, not consistently associated with vomiting and cannot be explained by another medical condition. Functional vomiting is defined as having one or more episodes of vomiting per week, which are not self-induced or related to an eating disorder or rumination and which cannot be explained by another medical condition. Patients may suffer from functional nausea alone, functional vomiting alone, or a combination of both.

For cyclic vomiting syndrome, new criteria have been added to the previous Rome III criteria. Episodes of vomiting should now be stereotypical in each patient, at least 2 episodes should occur within a 6-month period and the primary and most severe symptom should be vomiting rather than abdominal pain.

The diagnostic criteria for rumination syndrome have been revised including changing the name of the disorder (no longer ‘adolescent’ rumination syndrome, since it may also be present in younger children). The criteria no longer define regurgitation as ‘painless’ since children may have a concomitant functional abdominal pain disorder and because rumination may be triggered by a sensation of discomfort which may be relieved by the rumination behavior. Ruling out an eating disorder has now been added as a prerequisite for the diagnosis.

For aerophagia, the changes seem minor and semantic, but they are aimed at creating a more unambiguous criteria set. Previously, with Rome III, children with another FGID often fulfilled the criteria for aerophagia leading to overestimation of its prevalence. It is noteworthy that in the adult Rome IV criteria this diagnosis has been abandoned as it was considered to represent a mechanism of belching and abdominal bloating/distension rather than an actual FGID. However, the pediatric working committee believes that in children this is indeed a well-recognized condition [2].

2.2.2. Functional abdominal pain disorders

All functional abdominal pain disorders (FAPDs) – previously referred to as abdominal pain-predominant FGIDs – have undergone moderate to major changes. The criteria for functional dyspepsia have been expanded; this diagnosis no longer requires pain to be the chief complaint and children may suffer from one or more of the following symptoms: postprandial fullness, early satiation, epigastric pain or burning (not associated with defecation). In harmony with the adult criteria, two subtypes of functional dyspepsia are now recognized: postprandial distress syndrome and epigastric pain syndrome.

Similar to the adult Rome criteria, irritable bowel syndrome (IBS) can now be divided into subtypes reflecting the predominant stool pattern (IBS with constipation, IBS with diarrhea, IBS with constipation and diarrhea, and unspecified IBS). While the evidence for IBS subtypes in children is limited, the committee agreed that this concept might be useful for research purposes. Furthermore, the difference between functional constipation and IBS with constipation has been clarified. If a child suffers from constipation and abdominal pain related to defecation or a change in frequency/form of stools, the child should first be treated for constipation and, if despite successful treatment, the abdominal pain persists, the child should be considered to suffer from IBS with constipation. The previous Rome III criteria lacked clarity on this issue. The question whether IBS with constipation and constipation without abdominal pain exist at opposite ends of the same spectrum is not further addressed in the pediatric Rome IV publication.

The criteria of abdominal migraine are now consistent with the criteria for cyclic vomiting syndrome. Episodes of abdominal migraine should also be stereotypical, should occur at least twice within 6 months and abdominal pain should be the predominant symptom. This FAPD may occur alongside other FAPDs.

Two Rome III diagnoses, functional abdominal pain and functional abdominal pain syndrome, have been replaced by a new Rome IV diagnosis; functional abdominal pain – not otherwise specified (FAP-NOS). Children with FAP-NOS suffer from episodes of abdominal pain (at least 4 times a month), without sufficient criteria for IBS. The criteria for this disorder have been harmonized with the adult criteria and with other FAPD criteria.

2.2.3. Functional defecation disorders

No major changes have been adopted in the diagnoses of functional constipation and functional nonretentive fecal incontinence.
For both disorders, the time criterion has changed; patients need to fulfill the criteria for 1 month instead of 2 months. The justification for this change is that the 2-month interval may unduly delay treatment in some children and the time criterion is now harmonized with the criteria for neonates/toddlers.

2.3. Multidimensional clinical profile (MDCP)

One of the most exciting features of Rome IV involves the development of innovative educational materials, in particular the Multi-Dimensional Clinical Profile (MDCP) and the Interactive Clinical Decision Toolkit, a software program that incorporates the diagnostic algorithms and the MDCP. The MDCP is a case-based learning module that helps clinicians understand the complexity and dimensionality of FGIDs. For each case scenario, the MDCP identifies and classifies five components: the categorical Rome diagnosis (Category A), additional subclassifications leading to more specific treatments (Category B), the personal impact of the disorder on the patient (Category C), psychosocial influences (Category D), and physiological abnormalities or biomarkers (Category E). The MDCP makes the clinician think about illness severity, psychological comorbidity, and underlying pathophysiological mechanisms. By doing so, it allows clinicians to develop a tailored treatment, taking these factors into account. The core concept of the MDCP is that patients with the same diagnosis may not always benefit from the same treatment. For example, an IBS patient with mild symptoms of abdominal pain and loose stools who functions without impairment would be treated differently than a patient with the same diagnosis who suffers from severe disabling pain and has a comorbid anxiety disorder. Improved insights into the pathophysiology of FGIDs and associated psychosocial factors may help to improve this individualized approach in the future.

2.4. Novel insights into the pathophysiology and management of FGIDs

Even though in the last years there has been a fair amount of research on FGIDs in children, the pathophysiology of most FGIDs is still incompletely understood. This represents a limiting factor in better defining FGIDs and developing appropriate treatment strategies. The common consensus about the pathophysiology of FGIDs is that a multitude of influencing factors are involved. Genetic predisposition, impaired pain regulatory systems, sensory input (e.g. tissue damage, intestinal distension), psychological vulnerability, coping style, (family) stress, early life events, and environmental factors may all play a role in the multifactorial etiology of these disorders. Here, we will highlight two research areas which have received increasing attention over the past decade.

2.4.1. Brain–gut axis

One of the major developments of the past decade has been the improved understanding of the involvement of the brain–gut axis in FGIDs, particularly in FAPDs. It is now well recognized that bidirectional brain–gut interactions play an important role in gastrointestinal physiology and that alterations in these brain–gut interactions are likely to underlie symptoms of chronic abdominal pain and associated gastrointestinal dys-function [9]. This is supported by studies utilizing functional MRI, which have demonstrated structural and functional brain differences in adolescents with IBS compared with healthy subjects [10,11]. These results corroborate previous findings in adults with IBS and provide insights into the pathogenesis.

The role of brain–gut interactions in the pathophysiology of FAPDs also provides therapeutic opportunities. Recent trials with hypnotherapy for FAPDs have shown promising results [12,13]. Although the exact working mechanism of hypnotherapy for these disorders is still incompletely understood, it is hypothesized to exert effects on both physiological and psychological processes. In other words, hypnotherapy may have an effect on brain–gut interactions.

The brain–gut axis plays an important role in pain perception related to the gut. In young children, it is difficult to assess pain and validated measures of infant crying and chronic pain assessment are currently not available. The working committee has provided an overview of the current knowledge on the neurobiology in infants and toddlers and has recommended that such tools should be developed [1].

2.4.2. Gut microbiota

With the development of culture-independent analyzing techniques, our understanding of the role of the gut microbiota in health and disease has expanded extensively. Changes in the gut microbiota have been demonstrated in several organic diseases and functional disorders [14–16]. For some health problems, e.g. obesity, there is even evidence for a causal relationship, suggesting that the gut microbiota may play a role in the pathogenesis of these health problems [17]. This has led to an increased interest in ways to alter the gut microbiota and in the therapeutic value of prebiotics, probiotics, and symbiotics. Although the effects of these agents are poorly understood, there have been multiple trials investigating their efficacy in the treatment of a wide range of diseases and disorders, including FGIDs in children [18]. Currently, there is a limited amount of published data available for their use in pediatric FGIDs. The evidence suggests that specific probiotic strains may be beneficial in children with FAPDs [18], but for other FGIDs such as infant colic and functional constipation the evidence is ambiguous [19,20]. A better understanding of the role of the gut microbiota in FGIDs is required in order to develop novel tailored therapeutic approaches aimed at modulating the gut microbiota that may benefit patients with FGIDs. Furthermore, a better understanding of the gut microbiota in healthy children is of critical importance in order to improve our understanding of the role of the gut microbiota in pediatric FGIDs.

3. Conclusion

The Rome process and the validation and modification of the criteria have provided a platform for the improvement of the understanding and treatment of children with FGIDs. The most notable changes in Rome IV were made in the criteria for children/adolescents with the definition of functional nausea and functional vomiting and the modifications of the criteria for FAPDs. For the youngest age group, the criteria for infant
colic have undergone considerable modifications. Overall, the criteria for all disorders have become more specific, a fact which can be expected to enable clearer definition of patient populations for research purposes. Thus, with Rome IV, the road to an adequate classification of FGIDs in children has been repaved once more. A deeper understanding of the pathophysiologic mechanisms underlying FGIDs is necessary and should be one of the chief aims for future research. Novel insights into the role of influencing factors, such as the brain–gut axis and the microbiome, in the pathophysiology of FGIDs may improve our understanding of these disorders and could enhance management strategies by enabling a tailored therapeutic approach.

4. Expert commentary
Seventeen years after the first pediatric Rome criteria were launched, the framework for diagnosing FGIDs in children has been optimized and expanded. With new diagnoses and considerable changes and refinement to some of the existing diagnoses, Rome IV is expected to enhance diagnostic specificity. Nevertheless, it is unlikely that this will be the final version; future insights are likely to inspire the working committees to revise the Rome criteria again at some point in time.

Creating accurate and specific criteria sets for FGIDs is essential for adequate diagnoses, both in the clinical setting and in research. Adequate diagnoses allow the patients and families to embrace the problem, may prevent unnecessary investigations and limit healthcare costs. Creating specific criteria is dependent on the available evidence at that time. At the inception of the pediatric Rome II criteria, there was a paucity of literature regarding pediatric FGIDs and the criteria were primarily based on expert consensus. Nowadays, more published evidence has become available. With more literature becoming available, the Rome criteria are becoming increasingly evidence based.

Nevertheless, the Rome IV criteria have some limitations. One of the main difficulties in diagnosing FGIDs is that the clinician needs a reliable history. In (young) children, this can prove to be challenging. Symptoms such as nausea and abdominal pain are complex to describe and children may not be able to report these symptoms accurately. Furthermore, it is debatable whether all diagnoses included in Rome IV are truly clinical disorders and whether they are all related to the gastrointestinal tract. For instance, infant regurgitation is defined as an FGID, while in clinical practice this is considered to be a phenomenon that falls within the normal range and which resolves during the course of infancy. A recent study in the USA showed that the prevalence of infant regurgitation was 26% in the general population in children <12 months of age [7]. At the peak age for infant regurgitation (around 2–4 months of age), the prevalence has even been reported to be 67–87% [21,22]. So, if most infants have infant regurgitation and if it resolves spontaneously without treatment and is not associated with negative consequences, should it truly be characterized as a FGID? On the other hand, infant regurgitation is a frequent reason for parental concern and a common reason for a visit to the physician. Thus, it is understandable that the frequent occurrence and the accompanying parental concern have convinced the working committee to define this phenomenon in order to prevent unnecessary diagnostics or treatment. Another example of a disputable FGID is infant colic. The pathophysiologic mechanisms underlying this entity are incompletely understood and it is questionable if these symptoms are related to the gastrointestinal tract (which is suggested by the nomenclature). Other potential etiologic factors that have been suggested to be involved include psychosocial factors, neurodevelopmental features, dysbiosis of the gut microbiota, early life events, gastrointestinal motility and the type of feeding. Again, these symptoms may lead to uneasiness and fear among parents and many of these infants are indeed seen by the pediatric gastroenterologist. It is therefore understandable that the problem has been included in Rome IV, even though the relationship with the gut is questionable.

5. Five-year view
During the next 5–10 years, advances in research and resulting insights will likely improve our knowledge about the pathophysiology and treatment of FGIDs in children, which will probably lead to new attempts at improving the Rome criteria. Future revisions will likely result in further clarification and refining of the current criteria and the proposal of new entities. A better understanding of the pathophysiology of FGIDs may lead to the definition of other subtypes of FGIDs and these developments will likely mimic the recent developments in the adult Rome criteria, where cannabinoid or opioid-induced symptoms are now described. Furthermore, modern-day research may have a profound effect on the way we diagnose and treat FGIDs in children in the coming decade. Novel treatment strategies may involve new pharmacological agents, non-pharmacological therapies targeting the brain–gut axis (e.g. hypnotherapy, self-hypnosis, and yoga) and therapies targeting the gut microbiota (e.g. prebiotics, probiotics, and fecal transplants). The working committees have formulated recommendations for future research in both age groups. These recommendations are aimed at improving our understanding of the pathophysiology of FGIDs, exploring whether there are subtypes of known FGIDs, optimizing evaluation of children with FGIDs and thereby enabling a more tailored approach in treatment strategies. In addition, specific recommendations for research in children with IBS have recently been published by the Rome Foundation subcommittee for Pharmacological Clinical Trials in Children with IBS [23]. In the future, similar research recommendations should be provided for other FGIDs in order to improve comparability and reliability of pediatric FGID research. In addition, recent studies have shown that outcome measures often vary among studies [24,25], making it difficult to compare them with one another. Future efforts to provide uniform outcome measures should therefore be encouraged.
6. Key issues

- The symptom-based pediatric Rome IV criteria are used to diagnose FGIDs in children and should replace the Rome III criteria.
- Novel insights into the pathophysiology, evaluation and management of FGIDs have led to significant changes in the criteria.
- Three new FGIDs have been defined: functional nausea, functional vomiting and functional abdominal pain – not otherwise specified (FAP-NOS)
- For functional dyspepsia and irritable bowel syndrome, subtypes have been defined.
- Overall, the criteria for FGIDs have become more specific and some have been harmonized with criteria for other FGIDs or with the adult criteria.

Funding

This paper was not funded.

Declaration of interest

S. Nurko, M. Saps, C. Di Lorenzo and M.A. Benninga were part of the pediatric working committees of the Rome Foundation and have developed the Rome IV criteria discussed in this review. M. Saps is a scientific consultant for Forest, Quintiles, Ardeley, OQI Medical, IMHealth Science, Nutricia. C. Di Lorenzo is a scientific consultant QOL Medical, IMHealth Science, Merck, Nestlé. M.A. Benninga is a scientific consultant for Shire, Sucupica, AstraZeneca, Norgine, Zeria, Coloplast, Danone, Friesland Campina, Sensus, Novalac. The authors report no other relevant potential conflicts of interest.

References

Papers of special note have been highlighted as either of interest (∗) or of considerable interest (**) to readers.


** The Rome IV criteria for neonates/toddlers.


** The Rome IV criteria for children/adolescents.


** Study on the prevalence of functional gastrointestinal disorders in infants and toddlers.


** Recommendations from the Rome committee for future trials in children with irritable bowel syndrome.


Appendix 1. Childhood Functional Gastrointestinal Disorders: neonate/Toddler


G1. Diagnostic Criteria for Infant Regurgitation
Must include both of the following in otherwise healthy infants 3 weeks to 12 months of age:
(1) Regurgitation 2 or more times per day for 3 or more weeks
(2) No retching, hematemesis, aspiration, apnea, failure to thrive, feeding or swallowing difficulties, or abnormal posturing

G2. Diagnostic Criteria for Rumination Syndrome
Must include all of the following for at least 2 months:
(1) Repetitive contractions of the abdominal muscles, diaphragm, and tongue
(2) Effortless regurgitation of gastric contents, which are either expelled from the mouth or rechewed and reswallowed
(3) Three or more of the following:
   a. Onset between 3 and 8 months
   b. Does not respond to management for gastroesophageal reflux disease and regurgitation
   c. Unaccompanied by signs of distress
   d. Does not occur during sleep and when the infant is interacting with individuals in the environment

G3. Diagnostic Criteria for Cyclic Vomiting Syndrome
Must include all of the following:
(1) Two or more periods of unremitting paroxysmal vomiting with or without retching, lasting hours to days within a 6-month period
(2) Episodes are stereotypical in each patient
(3) Episodes are separated by weeks to months with return to baseline health between episodes of vomiting

G4. Diagnostic Criteria for Infant Colic
For clinical purposes, must include all of the following:
(1) An infant who is <5 months of age when the symptoms start and stop
(2) Recurrent and prolonged periods of infant crying, fussing, or irritability reported by caregivers that occur without obvious cause and cannot be prevented or resolved by caregivers
(3) No evidence of infant failure to thrive, fever, or illness

‘Fussing’ refers to intermittent distressed vocalization and has been defined as ‘[behavior] that is not quite crying but not awake and content either.’ Infants often fluctuate between crying and fussing, so that the 2 symptoms are difficult to distinguish in practice.

For clinical research purposes, a diagnosis of infant colic must meet the preceding diagnostic criteria and also include both of the following:
(1) Caregiver reports infant has cried or fussed for 3 or more hours per day during 3 or more days in 7 days in a telephone or face-to-face screening interview with a researcher or clinician
(2) Total 24-hour crying plus fussing in the selected group of infants is confirmed to be 3 h or more when measured by at least one prospectively kept, 24-hour behavior diary

G5. Diagnostic Criteria for Functional Diarrhea
Must include all of the following:
(1) Daily painless, recurrent passage of 4 or more large, unformed stools
(2) Symptoms last more than 4 weeks
(3) Onset between 6 and 60 months of age
(4) No failure to thrive if caloric intake is adequate

G6. Diagnostic Criteria for Infant Dyschezia
Must include in an infant <9 months of age:
(1) At least 10 min of straining and crying before successful or unsuccessful passage of soft stools
(2) No other health problems

G7. Diagnostic Criteria for Functional Constipation
Must include 1 month of at least 2 of the following in infants up to 4 years of age:
(1) 2 or fewer defecations per week
(2) History of excessive stool retention
(3) History of painful or hard bowel movements
(4) History of large-diameter stools
(5) Presence of a large fecal mass in the rectum

In toilet-trained children, the following additional criteria may be used:
(1) At least 1 episode/week of incontinence after the acquisition of toileting skills
(2) History of large-diameter stools that may obstruct the toilet
Appendix 2. Functional Gastrointestinal Disorders: children and Adolescents


H1a. Diagnostic Criteria for Cyclic Vomiting Syndrome
Must include all of the following:
(1) The occurrence of 2 or more periods of intense, unremitting nausea and paroxysmal vomiting, lasting hours to days within a 6-month period
(2) Episodes are stereotypical in each patient
(3) Episodes are separated by weeks to months with return to baseline health between episodes
(4) After appropriate medical evaluation, the symptoms cannot be attributed to another condition

H1b. Diagnostic Criteria* for Functional Nausea and Functional Vomiting
H1b1. Functional Nausea
Must include all of the following fulfilled for the last 2 months:
(1) Bothersome nausea as the predominant symptom, occurring at least twice per week, and generally not related to meals
(2) Not consistently associated with vomiting
(3) After appropriate evaluation, the nausea cannot be fully explained by another medical condition

H1b2. Functional Vomiting
Must include all of the following:
(1) On average, 1 or more episodes of vomiting per week
(2) Absence of self-induced vomiting or criteria for an eating disorder or rumination
(3) After appropriate evaluation, the vomiting cannot be fully explained by another medical condition

*Criteria fulfilled for at least 2 months before diagnosis.

H1c. Diagnostic Criteria* for Rumination Syndrome
Must include all of the following:
(1) Repeated regurgitation and rechewing or expulsion of food that
   a. Begins soon after ingestion of a meal
   b. Does not occur during sleep
(2) Not preceded by retching
(3) After appropriate evaluation, the symptoms cannot be fully explained by another medical condition. An eating disorder must be ruled out

*Criteria fulfilled for at least 2 months before diagnosis.

H1d. Diagnostic Criteria* for Aerophagia
Must include all of the following:
(1) Excessive air swallowing
(2) Abdominal distention due to intraluminal air which increases during the day
(3) Repetitive belching and/or increased flatus
(4) After appropriate evaluation, the symptoms cannot be fully explained by another medical condition.

*Criteria must be fulfilled for at least 2 months before diagnosis.

H2a. Diagnostic Criteria* for Functional Dyspepsia
Must include 1 or more of the following bothersome symptoms at least 4 days per month:
(1) Postprandial fullness
(2) Early satiation
(3) Epigastric pain or burning not associated with defecation
(4) After appropriate evaluation, the symptoms cannot be fully explained by another medical condition.

a Criteria fulfilled for at least 2 months before diagnosis.

Within FD, the following subtypes are now adopted:
(1) Postprandial distress syndrome includes bothersome postprandial fullness or early satiation that prevents finishing a regular meal. Supportive features include upper abdominal bloating, postprandial nausea, or excessive belching
(2) Epigastric pain syndrome, which includes all of the following: bothersome (severe enough to interfere with normal activities) pain or burning localized to the epigastrium. The pain is not generalized or localized to other abdominal or chest regions and is not relieved by defecation or passage of flatus. Supportive criteria can include (a) burning quality of the pain but without a retrosternal component and (b) the pain commonly induced or relieved by ingestion of a meal but may occur while fasting.

H2b. Diagnostic Criteria* for Irritable Bowel Syndrome
Must include all of the following:
(1) Abdominal pain at least 4 days per month associated with one or more of the following:
   a. Related to defecation
   b. A change in frequency of stool
   c. A change in form (appearance) of stool
(2) In children with constipation, the pain does not resolve with resolution of the constipation (children
   (3) in whom the pain resolves have functional constipation, not irritable bowel syndrome)
(4) After appropriate evaluation, the symptoms cannot be fully explained by another medical condition

(Continued)
Appendix 2. Continued.

**H2c. Diagnostic Criteria for Abdominal Migraine**

Must include all of the following occurring at least twice:

1. Paroxysmal episodes of intense, acute periumbilical, midline or diffuse abdominal pain lasting for 1 hour or more (should be the most severe and distressing symptom).
2. Episodes are separated by weeks to months.
3. The pain is incapacitating and interferes with normal activities.
4. Stereotyped pattern and symptoms in the individual patient.
5. The pain is associated with 2 or more of the following:
   - Anorexia
   - Nausea
   - Vomiting
   - Headache
   - Photophobia
   - Pallor
6. After appropriate evaluation, the symptoms cannot be fully explained by another medical condition.

Criteria fulfilled for at least 2 months before diagnosis.

**H2d. Diagnostic Criteria for Functional Abdominal Pain-NOS**

Must be fulfilled at least 4 times per month and include all of the following:

1. Episodic or continuous abdominal pain that does not occur solely during physiologic events (e.g., eating, menses).
2. Insufficient criteria for irritable bowel syndrome, functional dyspepsia, or abdominal migraine.
3. After appropriate evaluation, the abdominal pain cannot be fully explained by another medical condition.

Criteria fulfilled for at least 2 months before diagnosis.

**H3a. Diagnostic Criteria for Functional Constipation**

Must include 2 or more of the following occurring at least once per week for a minimum of 1 month with insufficient criteria for a diagnosis of irritable bowel syndrome:

1. 2 or fewer defecations in the toilet per week in a child of a developmental age of at least 4 years.
2. At least 1 episode of fecal incontinence per week.
3. History of retentive posturing or excessive volitional stool retention.
4. History of painful or hard bowel movements.
5. Presence of a large fecal mass in the rectum.
6. History of large diameter stools that can obstruct the toilet.

After appropriate evaluation, the symptoms cannot be fully explained by another medical condition.

**H3b. Diagnostic Criteria for Nonretentive Fecal Incontinence**

At least a 1-month history of the following symptoms in a child with a developmental age older than 4 years:

1. Defecation into places inappropriate to the sociocultural context.
2. No evidence of fecal retention.
3. After appropriate medical evaluation, the fecal incontinence cannot be explained by another medical condition.